Remarks

Claims 1-10 were previously pending in the subject application. By this Amendment, the applicants have amended claims 1, 4, 5, 9 and 10, have cancelled claims 2, 3 and 7 and have added new claim 11. Support for the amendments can be found throughout the subject specification and claims as originally filed. No new matter has been added by this Amendment. Accordingly, claims 1, 4-6 and 8-11 are currently before the Examiner. Favorable consideration of the claims now presented is respectfully requested.

The claim amendments set forth herein have been done in order to lend greater clarity to the claimed subject matter and to expedite prosecution. The amendment and cancellation of the claims should not be taken to indicate the applicants' agreement with, or acquiescence to, the rejections of record. Favorable consideration of the claims now presented, in view of the remarks and amendments set forth herein, is earnestly solicited.

Claim 9 has been rejected under 35 U.S.C. §112, second paragraph. The applicants respectfully traverse this ground for rejection to the extent that it might be applied to the amended claim 9 submitted herein. Please note that claim 9 has been amended to delete reference to "analogues," thereby addressing the issue raised by the Examiner. Accordingly, the applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §112, second paragraph.

Claims 1-5 and 7 have been rejected under 35 U.S.C. §102(b) as being anticipated by Mimoz *et al.* (Anaesthesia, June 2001, England, Vol. 56, no. 6, pages 520-525). The applicants respectfully traverse this ground for rejection because the Mimoz *et al.* reference does not disclose each and every element of the applicants' advantageous method as now claimed wherein single enantiomer (+)-nefopam is used to treat certain specified conditions.

In order to lend greater clarity to the claimed subject matter, the applicants' claims have been amended herein to recite the use of single enantiomer (+)-nefopam, and to further recite that the condition being treated is induced by chemotherapy, surgery or motion.

It is basic premise of patent law that, in order to anticipate, a single prior art reference must disclose within its four corners, each and every element of the claimed invention. In *Lindemann v.*

American Hoist and Derrick Co., 221 USPQ 481 (Fed. Cir. 1984), the court stated:

> Anticipation requires the presence in a single prior art reference, disclosure of each and every element of the claimed invention, arranged as in the claim. *Connell v. Sears Roebuck and Co.*, 722 F.2d 1542, 220 USPQ 193 (Fed. Cir. 1983); *SSIH Equip. S.A. v. USITC*, 718 F.2d 365, 216 USPQ 678 (Fed. Cir. 1983). In deciding the issue of anticipation, the [examiner] must identify the elements of the claims, determine their meaning in light of the specification and prosecution history, and identify corresponding elements disclosed in the allegedly anticipating reference. *SSIH, supra*; *Kalman [v. Kimberly-Clarke*, 713 F.2d 760, 218 USPQ 781 (Fed. Cir. 1983)] (emphasis added). 221 USPQ at 485.

Please note that the Mimoz *et al.* reference does not disclose the use of single enantiomer (+)-nefopam for the treatment of nausea, dizziness, blurred vision or emesis wherein the condition is induced by chemotherapy, surgery or motion. Because the claimed subject matter is not disclosed by Mimoz *et al.*, there is no anticipation. Accordingly, the applicants respectfully request reconsideration and withdrawal of the rejection under 35 USC §102(b) based on the Mimoz *et al.* reference.

Claims 1-5 and 7 have been rejected under 35 U.S.C. §102(b) as being anticipated by McLintock *et al.* (Br. J. Surg., August 1988, Vol. 75, pages 779-781). The applicants respectfully traverse this ground for rejection because the McLintock *et al.* reference does not disclose each and every element of the applicants' advantageous method as now claimed.

As noted above, in order to lend greater clarity to the claimed subject matter, the applicants' claims have been amended herein to recite the use of single enantiomer (+)-nefopam, and to further recite that the condition being treated is induced by chemotherapy, surgery or motion.

Please note that the McLintock *et al.* reference does not disclose the use of (+)-nefopam for the treatment of nausea, dizziness, blurred vision or emesis that is induced by chemotherapy, surgery or motion. Because the claimed subject matter is not disclosed by McLintock *et al.*, there is no anticipation. Accordingly, the applicants respectfully request reconsideration and withdrawal of the rejection under 35 USC §102(b) based on the McLintock *et al.* reference

Claims 1, 5 and 6 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Mimoz *et al.* in view of Sridhar *et al.* (Cancer, April 15, 1988, Vol. 61, no 8, pages 1508-1517). The

applicants respectfully traverse this ground for rejection because the cited references, either taken alone or in combination, do not disclose or suggest the applicants' treatment method as claimed herein.

In making this rejection, the Office Action relies on Mimoz *et al.* as teaching that nefopam is an anti-emetic agent. As discussed below, the applicants respectfully disagree with this interpretation of the teachings of Mimoz *et al.* In fact, those skilled in the art at the time of this invention knew that nausea and vomiting were well known side-effects associated with nefopam. See, for example, Pillans, P.I. *et al.* ("Adverse reactions associated with nefopam," The New Zealand Medical Journal, September 22, 1995, Vol. 108, No, 1008) (R6); Ghose, K. *et al.* ("An open pilot study of the preventive effect of nefopam in migraine headaches," Headache Quarterly, 1999, United States, Vol. 10, no. 3, pages 221-224, ISSN:1059-7565) (R2); and Lasseter, K.C. *et al.* ("Nefopam HCl interaction study with eight other drugs," Journal of International Medical Research, 1976, Vol. 4, No. 3, pages 195-201) (R3).

The Office Action suggests that nefopam reduces nausea and vomiting associated with other drugs, e.g. morphine. Although it may be true that nefopam can be used in conjunction with morphine in a way that results in a reduction of side effects, the correct interpretation of the teachings of Mimoz *et al.* is that any reduction in nausea or vomiting is the consequence of a reduced dosage of morphine. It cannot be concluded from the cited reference that nefopam is anti-emetic, and indeed that would be inconsistent with the teachings found in prior art references.

Accordingly, there is no evidence in the prior art that racemic nefopam, much less (+)-nefopam, is anti-emetic. In fact, as noted above, nausea and vomiting are well-documented as deleterious side effects of racemic nefopam. Furthermore, because (+)-nefopam is generally considered to be more potent than (-)-nefopam (see, for example, Fasmer *et al., J. Pharm. Pharmacol.* 42(6):437-438, 1987; Rosland and Hole, *J. Pharm. Pharmacol.* 42(6):437-438, 1990; and Mather *et al., Chirality* 12(3):153-159, 2000) (copies enclosed), the only reasonable conclusion to be drawn from the prior art is that (+)-nefopam would be strongly pro-emetic. Therefore, it is very surprising that (+)-nefopam can be used according to the subject invention to actually treat nausea, dizziness, blurred vision and emesis.

It is well established in the patent law that the mere fact that the purported prior art could have been modified or applied in some manner to yield an applicant's invention does not make the modification or application obvious unless "there was an apparent reason to combine the known elements in the fashion claimed" by the applicant. *KSR International Co. v. Teleflex Inc.*, 550 U.S. ___ (2007). Furthermore, an applicant's invention is not "proved obvious merely by demonstrating that each of its elements was, independently, known in the (purported) prior art." *Id.*

In view of the fact that the prior art, including the Mimoz *et al* .reference, did not teach that nefopam was an anti-emetic agent, there would be no reason for the skilled artisan to combine the teachings of Mimoz *et al.* and Sridhar *et al.* to arrive at the current invention.

It is also important to appreciate that the present invention does not involve the use of a single enantiomer, instead of the racemate, in a therapeutic application which is already known. To the contrary, the racemic was actually contraindicated for the use that is now claimed for the single enantiomer. The present invention is, in fact, contrary to every indication provided in the prior art. The discovery that (+)- is anti-emetic is genuinely surprising.

The cited references do not disclose or suggest the advantageous use of single enantiomer (+)-nefopam as now claimed by the current applicants. Accordingly, the applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §103 based on the Mimoz *et al.* reference in view of the teachings of Sridhar *et al.*.

Claims 1 and 8-10 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Mimoz *et al.* in view of Sridhar *et al.* (Cancer, April 15, 1988, Vol. 61, no 8, pages 1508-1517). The applicants respectfully traverse this ground for rejection because the cited references, taken either alone or in combination, do not disclose or suggest the applicants' treatment method as claimed herein.

The shortcomings of the cited references, as those references related to the current invention have been discussed above in detail. Specifically, these references provide no expectation that single enantiomer (+)-nefopam could be used to treat nausea, dizziness, blurred vision or emesis as claimed by the current applicants. In fact, this use is contrary to reports in the prior art that attribute these

same unwanted side effects to the use of nefopam.

As noted above, the mere fact that the purported prior art could have been modified or applied in some manner to yield applicant's invention does not make the modification or application obvious unless the prior art suggested the desirability of the modification. *In re Gordon*, 221 USPQ 1125,1127 (Fed. Cir. 1984). An assertion of obviousness without the required suggestion or expectation of success in the prior art is tantamount to using applicant's disclosure to reconstruct the prior art to arrive at the subject invention. Hindsight reconstruction of the prior art cannot support a §103 rejection, as was specifically recognized by the CCPA in *In re Sponnoble*, 56CCPA 823, 160 USPQ 237, 243 (1969).

As discussed in detail above, the Mimoz *et al.* reference does not teach that nefopam is an anti-emetic agent. In fact, the prior art as a whole, suggested quite the opposite. Thus, the cited references do not suggest the desirability of the method claimed by the current applicants and provide no expectation of successful use of (+)-nefopam in treatment of nausea, dizziness, blurred vision and emesis. Accordingly, the applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §103 based on the Mimoz *et al.* reference in view of Sridhar *et al.*.

In view of the foregoing remarks, the applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 CFR §§1.16 or 1.17 as required by this paper to Deposit Account No. 19-0065.

The applicants also invites the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephone interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,

David Saliwanchik

David R. Saliwanchik
Patent Attorney
Registration No. 31,794
Phone: 352-375-8100
Fax No.: 352-372-5800
Address: P.O. Box 142950
Gainesville, FL 32614-2950

DRS/la